

## Claims

What is claimed is:

1. Apparatus for determining a characteristic of a sample of material by the interaction of electromagnetic radiation with the sample, comprising:

a source of electromagnetic radiation;

illuminating optics for sequentially illuminating a plurality of volume elements in the sample with an intensity distribution in the sample that drops off substantially monotonically from a first region in a first optical path;

collecting optics for collecting electromagnetic radiation emanating from each of said volume elements, said collecting optics collecting said electromagnetic radiation emanating from each of said volume elements with a collection distribution that drops off substantially monotonically from a second region in a second optical path, said first and second regions at least partially overlapping in each of said volume elements, said illuminating and collecting optics each having respective field stops whose dimensions are large compared to a quotient of wavelength of said electromagnetic radiation divided by a working numerical aperture of said illuminating and collecting optics, respectively, measured from said respective field stops; and

a detector for detecting the collected electromagnetic radiation emanating from each of said sequentially illuminated volume elements to produce a response representative of said characteristic in each of said volume elements,

wherein the sample of material comprises a biological tissue.

2. Apparatus as defined in claim 1 wherein at least one of the illuminating and the collecting optics comprises means for determining said characteristic from a three dimensional array of said volume elements.

3. Apparatus as defined in claim 1 wherein the field stops of said illuminating optics comprises an array of individually controllable illuminating optical shutters for sequentially illuminating said volume elements.

4. Apparatus as defined in claim 3 wherein the field stops of said collecting optics comprises an array of individually controllable collection optical shutters for sequentially collecting electromagnetic radiation emanating from each of said volume elements.

5. Apparatus as defined in claim 1 wherein said illuminating optics comprises an array of individually controllable illuminating elements for sequentially illuminating said volume elements and said collecting optics comprises an array of individually controllable collection elements for sequentially collecting electromagnetic radiation emanating from each of said volume elements.

6. Apparatus for determining a characteristic of a sample of material by the interaction of electromagnetic radiation with the sample, comprising:

- a source of electromagnetic radiation;
  - an optical assembly for sequentially illuminating a plurality of volume elements in the sample with an intensity distribution in the sample that drops off substantially monotonically from a first region in a first optical path and for collecting electromagnetic radiation emanating from each of said volume elements, said optical assembly collecting said electromagnetic radiation emanating from each of said volume elements with a collection distribution that drops off substantially monotonically from a second region in a second optical path, said first and second regions at least partially overlapping in each of said volume elements, said optical assembly comprising at least one array of field stops whose dimensions are large compared to a quotient of wavelength of said electromagnetic radiation divided by a working numerical aperture of said optical assembly, measured from said field stops; and
  - a detector for detecting the collected electromagnetic radiation emanating from each of said sequentially illuminated volume elements to produce responses representative of said characteristic in each of said volume elements,
- wherein said sample comprises a biological tissue.

7. Apparatus as defined in claim 6 wherein said array of field stops comprises a single array of individually controllable optical shutters for sequentially illuminating said volume elements and for sequentially collecting electromagnetic radiation emanating from each of said volume elements, wherein said first and second optical paths are the same.

8. Apparatus as defined in claim 7 wherein said array of optical shutters comprises an array of individually controllable liquid crystal shutter elements.

9. Apparatus as defined in claim 7 wherein said array of optical shutters comprises an array of individually controllable polymer dispersed liquid crystal shutter elements.

10. Apparatus as defined in claim 7 wherein said array of optical shutters comprises an array of individually controllable ferroelectric shutter elements.

11. Apparatus as defined in claim 7 wherein said array of optical shutters comprises an array of individually controllable piezoelectric bimorph shutter elements.

12. Apparatus as defined in claim 7 wherein said array of optical shutters comprises a micromachined array of individually controllable, electrostatically movable shutter elements.

13. Apparatus as defined in claim 6 further including means for moving at least a portion of said optical assembly with respect to the sample so as to vary the locations of said volume elements within the sample along the optical axis of said first and second optical paths.

14. Apparatus as defined in claim 7 wherein said optical assembly further includes an optical objective between said array of optical shutters and the sample.

15. Apparatus as defined in claim 14 wherein said optical objective comprises a single objective lens aligned with said array of optical shutters.

16. Apparatus as defined in claim 14 wherein said optical objective comprises an array of microlens elements respectively aligned with said optical shutters.

17. Apparatus as defined in claim 7 wherein said array of optical shutters is subdivided into noninterfering zone arrays and electromagnetic radiation is collected simultaneously from said noninterfering zone arrays.

18. Apparatus as defined in claim 7 wherein said array of optical shutters comprises a plurality of rows and columns of shutter elements.

19. Apparatus as defined in claim 7 wherein said array of optical shutters comprises an array of radially distributed shutter elements.

20. Apparatus as defined in claim 7 wherein said array of optical shutters comprises a linear array of shutter elements.

21. Apparatus as defined in claim 7 wherein said array of optical shutters comprises a circumferential array of shutter elements.

22. Apparatus as defined in claim 6 wherein said array of field stops comprises an array of individually movable micromirrors, each of said micromirrors being movable between an active position for directing illumination from said source to the sample and for directing collected electromagnetic radiation from the sample to said detector, and an inactive position.

23. Apparatus as defined in claim 6 wherein said array of field stops comprises an array of individually movable micromirrors, each of said micromirrors comprising an off axis segment of a paraboloid of revolution, said micromirrors being movable in pairs between active positions and inactive positions, one micromirror of an active pair directing illumination from said source to the sample and the other micromirror of the active pair directing electromagnetic radiation emanating from the sample to said detector.

24. Apparatus as defined in claim 23 wherein micromirrors of a first group of said micromirrors sequentially direct illumination from said source to the sample and micromirrors of a second group of said micromirrors sequentially direct collected electromagnetic radiation from the sample to said detector.

25. Apparatus as defined in claim 23 wherein said array of field stops further comprises means for moving each of said micromirrors between an illumination position for directing illumination from said source to the sample and a collection position for directing collected electromagnetic radiation from the sample to said detector, wherein each of said micromirrors is used for illumination and collection at different times.

26. Apparatus as defined in claim 6 wherein said optical assembly comprises a bundle of optical fibers and an optical fiber switching device for sequentially activating each of said optical fibers for directing illumination from said source to the sample and for directing collected electromagnetic radiation from the sample to said detector.

27. Apparatus as defined in claim 6 wherein said optical assembly comprises a bundle of optical fibers and an array of optical shutters positioned at one end of said bundle of optical fibers so that said optical shutters are respectively aligned with said optical fibers, said array of optical shutters sequentially illuminating said volume elements and sequentially collecting electromagnetic radiation emanating from each of said volume elements.

28. Apparatus as defined in claim 6 wherein said detector comprises a single optical detector for detecting collected electromagnetic radiation from each of said volume elements.

29. Apparatus as defined in claim 7 wherein said detector comprises a plurality of detector elements corresponding to said optical shutters or to groups of said optical shutters.

30. Apparatus as defined in claim 6 wherein said source comprises a laser source.

31. Apparatus as defined in claim 6 wherein said source comprises a nitrogen laser.

32. Apparatus as defined in claim 6 wherein said source comprises a broad spectral band light source.

33. Apparatus as defined in claim 32 wherein said source comprises a xenon discharge lamp.

34. Apparatus as defined in claim 32 wherein said source comprises a halogen incandescent lamp.

35. Apparatus as defined in claim 6 wherein said source comprises an ultraviolet wavelength source.

36. Apparatus as defined in claim 6 wherein said optical assembly includes an optical filter for tailoring the spectrum of the illumination.

37. Apparatus as defined in claim 6 wherein said source comprises a plurality of light sources and means for activating said light sources at different times.

38. Apparatus as defined in claim 6 wherein said optical assembly further includes means for modulating the illumination of the sample.

39. Apparatus as defined in claim 6 wherein said response comprises natural  
5 fluorescence of tissue after illumination by a narrow wavelength excitation.

40. Apparatus as defined in claim 6 wherein said response is produced by selectively absorbed dye in pathological tissue.

10 41. Apparatus as defined in claim 6 wherein said detector comprises means for detecting responses produced by Raman scattering.

42. Apparatus as defined in claim 6 wherein said detector comprises means for detecting a combination of backscattering and reflection from said volume elements.

15 43. Apparatus as defined in claim 6 wherein said at least one array of field stops comprises an array of individually controllable illuminating optical shutters for sequentially illuminating said volume elements and an array of individually controllable collection optical shutters for sequentially collecting electromagnetic radiation emanating from each of said  
20 volume elements, and wherein said optical assembly further comprises illuminating light conditioning optics for directing illumination from said source to said array of illuminating optical shutters, an illuminating objective for focusing illumination on said volume elements, a collection objective for focusing said collection optical shutters on said volume elements and collection light conditioning optics for directing said collected electromagnetic radiation  
25 from said array of collection optical shutters to said detector.

44. Apparatus as defined in claim 6 wherein said at least one array of field stops comprises an array of individually controllable illuminating optical shutters for sequentially illuminating said plurality of volume elements and an array of individually controllable  
30 collection optical shutters for sequentially collecting electromagnetic radiation emanating from each of said volume elements.

45. Apparatus as defined in claim 44 wherein said array of illuminating optical shutters and said array of collection optical shutters each comprises an array of individually controllable liquid crystal shutter elements.

5 46. Apparatus as defined in claim 44 wherein said array of illuminating optical shutters and said array of collection optical shutters each comprises an array of individually controllable polymer dispersed liquid crystal shutter elements.

10 47. Apparatus as defined in claim 44 wherein said array of illuminating optical shutters and said array of collection optical shutters each comprises an array of individually controllable ferroelectric shutter elements.

15 48. Apparatus as defined in claim 44 wherein said array of illuminating optical shutters and said array of collection optical shutters each comprises an array of individually controllable piezoelectric bimorph shutter elements.

20 49. Apparatus as defined in claim 44 wherein said array of illuminating optical shutters and said array of collection optical shutters each comprises a micromachined array of individually controllable, electrostatically movable shutter elements.

50. Apparatus as defined in claim 44 wherein said optical assembly further includes a single illuminating objective lens between said array of illuminating optical shutters and the sample, and a single collection objective lens between the sample and said array of collection optical shutters.

25 51. Apparatus as defined in claim 44 wherein said optical assembly further includes an array of illuminating objective microlens elements respectively aligned with the optical shutters of said array of illuminating optical shutters and positioned between said array of illuminating optical shutters and the sample, and an array of collection objective  
30 microlens elements respectively aligned with the optical shutters of said array of collection



optical shutters and positioned between the sample and said array of collection optical shutters.

52. Apparatus as defined in claim 44 wherein said array of illuminating optical  
5 shutters and said array of collection optical shutters are subdivided into noninterfering zone  
arrays and electromagnetic radiation is collected simultaneously from said noninterfering  
zone arrays.

53. Apparatus as defined in claim 44 wherein said array of illuminating optical  
10 shutters and said array of collection optical shutters each comprises a plurality of rows and  
columns of shutter elements.

54. Apparatus as defined in claim 44 wherein said array of illuminating optical  
shutters and said array of collection optical shutters each comprises an array of radially  
15 distributed shutter elements.

55. Apparatus as defined in claim 44 wherein said array of illuminating optical  
shutters and said array of collection optical shutters each comprises a linear array of shutter  
elements.

56. Apparatus as defined in claim 44 wherein said array of illuminating optical  
shutters and said array of collection optical shutters each comprises a circumferential array of  
shutter elements.

57. Apparatus as defined in claim 6 wherein said optical assembly comprises  
25 illuminating optics for sequentially illuminating said plurality of volume elements and  
collecting optics for collecting electromagnetic radiation emanating from each of said volume  
elements, said illuminating optics comprising an illuminating bundle of optical fibers and  
illuminating control means for sequentially activating each of said optical fibers for directing  
30 illumination from said source to the sample, said collecting optics comprising a collection  
bundle of optical fibers and collection control means for sequentially activating each of said

optical fibers in said collection bundle for directing collected electromagnetic radiation from the sample to said detector.

58. Apparatus as defined in claim 57 wherein said illuminating control means comprises a first rotating mirror for sequentially directing illumination into the optical fibers of said illumination bundle and wherein said collection control means comprises a second rotating mirror for sequentially directing collected electromagnetic radiation from the optical fibers of said collection bundle to said detector.

59. Apparatus as defined in claim 57 wherein said illuminating control means comprises an array of individually controllable illuminating optical shutters respectively aligned with the optical fibers of said illuminating bundle and wherein said collection control means comprises an array of individually controllable collection optical shutters respectively aligned with the optical fibers of said collection bundle.

60. Apparatus as defined in claim 6 further comprising a spectral analyzer disposed between said optical assembly and said detector.

61. Apparatus as defined in claim 6 further comprising a temporal interferometer disposed between said optical assembly and said detector.

62. Apparatus as defined in claim 6 further comprising a spatial interferometer disposed between said optical assembly and said detector.

63. Apparatus as defined in claim 6 further comprising a Hadamard encodement mask disposed between said optical assembly and said detector.

64. A method for determining a characteristic of a sample of material by the interaction of electromagnetic radiation with the sample, comprising the steps of:  
providing an optical assembly adapted for positioning in proximity to the sample, wherein the sample comprises a biological tissue,

sequentially illuminating, with an optical assembly, a plurality of volume elements in the sample by directing electromagnetic radiation into the sample with an intensity distribution in the sample that drops off substantially monotonically from a first region in a first optical path;

5 sequentially collecting, with said optical assembly, electromagnetic radiation emanating from each of said sequentially illuminated volume elements with a collection distribution that drops off substantially monotonically from a second region in a second optical path, said first and second regions at least partially overlapping in each of said volume elements, said optical assembly comprising at least one array of field stops whose dimensions  
10 are large compared to a quotient of wavelength of said electromagnetic radiation divided by a working numerical aperture of said optical assembly, measured from said field stops; and

detecting the collected electromagnetic radiation emanating from each of said sequentially illuminated volume elements to produce a response representative of said characteristic in each of said volume elements.

15 65. A method as defined in claim 64 wherein the steps of sequentially illuminating and sequentially collecting are performed with said optical assembly, wherein said at least one array of field stops comprises a single array of individually controllable optical shutters.

20 66. A method as defined in claim 64 wherein said method further includes the step of moving at least a portion of said optical assembly with respect to the sample so as to vary the locations of said volume elements within the sample along the optical axis of said first and second optical paths.

25 67. A method as defined in claim 64 wherein the step of illuminating a plurality of volume elements includes simultaneously illuminating two or more noninterfering volume elements and wherein the step of collecting electromagnetic radiation includes simultaneously collecting electromagnetic radiation emanating from said noninterfering volume elements.

68. A method as defined in claim 64 wherein said array of field stops comprises an array of individually movable micromirrors, said method further comprising sequentially moving the micromirrors of said array between an active position for directing illumination to the sample and for directing collected electromagnetic radiation from the sample to a  
5 detector, and an inactive position.

69. A method as defined in claim 64 wherein said array of field stops comprises an array of individually movable micromirrors, each of said micromirrors comprising an off axis segment of a paraboloid of revolution, said method further comprising moving pairs of  
10 said micromirrors between active positions and inactive positions, one micromirror of an active pair directing illumination to the sample and the other micromirror of the active pair directing electromagnetic radiation emanating from the sample to a detector.

70. A method as defined in claim 64 wherein the step of illuminating a plurality of  
15 volume elements includes directing illumination through a bundle of illuminating optical fibers.

71. A method as defined in claim 64 wherein the step of collecting  
20 electromagnetic radiation includes directing collected electromagnetic radiation through a bundle of collection optical fibers.

72. A method as defined in claim 64 wherein the step of illuminating a plurality of volume elements includes modulating the illumination of the sample.

73. A method as defined in claim 64 wherein the steps of sequentially illuminating  
25 and sequentially collecting are performed with said optical assembly, wherein said at least one array of field stops comprises an array of individually controllable illuminating optical shutters and an array of individually controllable collection optical shutters.

74. A method as defined in claim 64 wherein the steps of sequentially illuminating  
30 and sequentially collecting are performed with said optical assembly, wherein said at least

one array of field stops comprises an array of individually controllable illuminating elements and an array of individually controllable collection elements.

75. A method as defined in claim 64 wherein the step of illuminating a plurality of volume elements includes illuminating said volume elements at different times with sources having different spectra.

76. A method as defined in claim 64 wherein the step of detecting the collected electromagnetic radiation is performed by an array of detector elements.

77. Apparatus as defined in claim 1 wherein the illuminating optics, the collecting optics and the detector include means for producing a response representative of a characteristic of biological tissue.

78. Apparatus as defined in claim 1 wherein said source, said illuminating optics, said collecting optics and said detector are configured for determining said characteristic in vitro.

79. Apparatus as defined in claim 1 wherein said source, said illuminating optics, said collecting optics and said detector are configured for determining said characteristic in vivo.

80. Apparatus as defined in claim 1 wherein said detector includes means for producing a response representative of at least one pathology.

81. Apparatus as defined in claim 1 wherein said detector includes means for producing a response representative of cancer.

82. Apparatus as defined in claim 80 further including means for presenting the response as an image of the spatial distribution of said at least one pathology.

83. A method as defined in claim 64 wherein the steps of sequentially illuminating, sequentially collecting and detecting are carried out with biological tissue as the sample.

5 84. A method as defined in claim 64 wherein the steps of sequentially illuminating, sequentially collecting and detecting are carried out in vitro.

85. A method as defined in claim 64 wherein the steps of sequentially illuminating, sequentially collecting and detecting are carried out in vivo.

10 86. A method as defined in claim 64 wherein the step of detecting includes producing a response representative of at least one pathology.

15 87. A method as defined in claim 64 wherein the step of detecting includes producing a response representative of cancer.

88. A method as defined in claim 86 further including the step of presenting the response as an image of the spatial distribution of at least one pathology.

20 88. Apparatus as defined in claim 1 wherein said biological tissue comprises an in vivo biological tissue.

89. Apparatus as defined in claim 88 further comprising a housing adapted for introducing said illuminating optics and said collecting optics into proximity to said in vivo biological tissue.

90. Apparatus as defined in claim 89 wherein said housing is adapted for permitting only a single intervention whereby said illuminating optics and said collecting optics are introduced into proximity to said in vivo biological tissue.

91. Apparatus as defined in claim 90 wherein said housing is adapted for being disposed of after use.

92. Apparatus as defined in claim 6 wherein said biological tissue comprises an in vivo biological tissue.

93. Apparatus as defined in claim 92 further comprising a housing adapted for introducing said optical assembly into proximity to said in vivo biological tissue.

94. Apparatus as defined in claim 93 wherein said housing is adapted for permitting only a single intervention whereby the optical assembly is introduced into proximity to said in vivo biological tissue.

95. Apparatus as defined in claim 94 wherein said housing is adapted for being disposed of after use.

96. Apparatus for covering an optical assembly, comprising:  
a sheath positioned external to a surface of the optical assembly, whereby the sheath is interposed between the surface of the optical assembly and a biological tissue; and  
a region in the sheath adapted for the transmission of optical signals between the optical assembly and the biological tissue.

97. Apparatus as defined in claim 96 wherein the region in the sheath is configured as a window.

98. Apparatus as defined in claim 97 wherein the window is in contact with the optical assembly.

99. Apparatus as defined in claim 96 wherein the sheath comprises a region shaped as a cylinder.

100. Apparatus as defined in claim 96 wherein the sheath is adapted for a single use.

101. Apparatus as defined in claim 96 further comprising a fastening mechanism whereby the sheath can be attached to the optical assembly.

102. Apparatus as defined in claim 101 wherein the fastening mechanism is adapted for preventing the sheath from being used with the optical assembly on more than one occasion.

103. A method for diagnosing a biological tissue, comprising:  
providing an optical assembly dimensionally adapted for positioning in proximity to a biological tissue;  
providing a sheath adapted for covering a surface of the optical assembly, wherein the sheath is capable of transmitting optical signals between the optical assembly and the biological tissue;  
positioning the sheath around the optical assembly so that the sheath is interposed between the optical assembly and the biological tissue;  
placing the optical assembly in juxtaposition to the biological tissue for a diagnosis thereof;

sequentially illuminating, with an optical assembly, a plurality of volume elements in the biological tissue by directing electromagnetic radiation into the biological tissue with an intensity distribution in the biological tissue that drops off substantially monotonically from a first region in a first optical path;

sequentially collecting, with said optical assembly, electromagnetic radiation emanating from each of said sequentially illuminated volume elements with a collection distribution that drops off substantially monotonically from a second region in a second optical path, said first and second regions at least partially overlapping in each of said volume elements, said optical assembly comprising at least one array of field stops whose dimensions are large compared to a quotient of wavelength of said electromagnetic radiation divided by a working numerical aperture of said optical assembly, measured from said field stops; and



detecting the collected electromagnetic radiation emanating from each of said sequentially illuminated volume elements to produce a response representative of said characteristic in each of said volume elements.

- 5            104. A method according to claim 103 further comprising attaching the sheath to the optical assembly with a fastening mechanism.